Remarks

Claims 1-3, 11-15, 17, and 29-32 were pending in this application. Claims 1, 3, 14, 30, and 32 are amended herein. Claims 2 and 12 are canceled herein without prejudice. New claims 33 and 34 are added. Therefore after entry of this amendment, claims **1, 3, 11, 13-15, and 29-34** are pending. Consideration and allowance of the pending claims is requested.

Telephone Interview

Applicants thank Examiner Nguyen for the courtesy of a telephone interview with their representative, Susan W. Graf, on January 27, 2011. During the telephone interview, the rejections under 35 U.S.C. § 103 and potential claim amendments were discussed to address the rejections were discussed. Though complete agreement was not reached, Applicants believe that this amendment addresses the concerns that were discussed regarding the § 103 rejections.

Double Patenting

Claims 1-3, 11-13, and 29-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 6-8 of Application No. 10/596,704. That application is now abandoned, rendering this rejection moot. Applicants request withdrawal of this rejection.

Claim Rejections – 35 U.S.C. § 103

Claims 1-3, 11-13, and 29-32 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chan *et al.* (U.S. 2002/0192690) in view of Hirabayashi *et al.* (*J. Chromatography A* 890:261-271, 2000) and Mir (U.S. 2004/0248144). Applicants request reconsideration in light of the amendments and arguments presented herein.

The Office asserts that it would have been obvious to one of skill in the art to detect the binding event taught by Chan *et al.* using evanescent wave excitation, as taught by Mir (Office action, page 6, first full paragraph). The Office also asserts that one of skill in the art would have had a reasonable expectation of success in utilizing the digitizing and quantifying method of Mir to detect fluorescently labeled glycoproteins in the method of Chan *et al.* because Hirabayashi *et*

al. discloses that fluorescence-based detection increases sensitivity of such methods (Office action, page 6, first full paragraph).

Claim 1 is amended herein to recite "a glass substrate onto which a protein that interacts with a sugar chain has been immobilized, wherein the glass substrate is coated with a compound comprising an epoxy group as an active group, and wherein a number of reaction vessels are formed on the glass substrate by affixing a rubber having a number of holes on the glass substrate..." in part (a) and to recite "measuring the intensity of an excited fluorescence after applying an evanescent wave generated by injecting an excitation light from the edge of the glass substrate, without washing the glass substrate" in part (b). Support for these amendments is found in the specification at least at page 5, lines 33-36; page 6, lines 18-20; page 12, lines 6-7; page 14, lines 23-34; page 23, lines 17-23; and original claim 2. Claims 2 and 12 are canceled herein in light of this amendment and claims 3 and 30 are amended to depend from claim 1. New claim 33 is added, which recites "wherein the rubber is a black silicon rubber." Support for this claim is found in the specification at least at page 22, lines 30-34.

Chan *et al.* disclose a porous semiconductor substrate and one or more coupled probes (*e.g.,* Chan, Abstract and paragraph [0013]) wherein an interaction between a coupled probe and a target molecule results in a change in the refractive index of the semiconductor substrate (*e.g.,* Chan, paragraph [0066]). Applicants emphasize that the pending claims recite a "glass substrate," as distinct from the semiconductor (silicon) substrate of Chan *et al.* Mir generally discloses that evanescent waves can be used in detecting a fluorescent signal (Mir, paragraph [0225]). In particular, Mir describes an example of detecting fluorescence generated by an evanescent wave wherein the fluorescence is collected using an x100 oil immersion objective lens (Mir, paragraph [0497]). If the porous semiconductor substrate was utilized in the method of Mir, an ideal evanescent wave would not be generated and the binding event would not be detected. This is because the presence of numerous discontinuous channels in the porous silicon would cause irregular reflection of the excitation light and result in stray light, rather than formation of an evanescent wave. Therefore, the combination of Chan *et al.* and Mir is inoperable, and one of skill in the art would not have a reasonable expectation of success in arriving at the claimed invention.

As shown in the Declaration under 37 C.F.R. § 1.132 signed by Dr. Jun Hirabayashi (Declaration) submitted herewith, the claimed method results in increased sensitivity of detection of an interaction between a sugar chain and a protein that interacts with a sugar chain as compared to current methods utilizing a confocal scanner (*e.g.,* paragraphs 6-8). As shown in **Exhibit C**, the claimed method provided higher levels of signal (9604 as compared to 1500) from a fluorescently-labeled glycan bound to a lectin on a microarray. This increased sensitivity occurred utilizing 10-fold lower concentration (10 nM as compared to 100 nM) of the probe than in the conventional confocal detection method. Thus, the claimed methods provide an unexpected increase in sensitivity over methods described in the cited references (such as Mir).

In addition, the claimed methods provide an increase in sensitivity over conventional methods which include a washing step (Declaration, paragraphs 9-11 and **Exhibit D**). Finally, the claimed method allows real-time detection of interactions of a sugar chain and a protein that interacts with a sugar chain, including both association and dissociation of the sugar chain and the protein that interacts with the sugar chain (Declaration, paragraphs 12-13 and **Exhibit E**). The claimed method is easier, faster, more sensitive, and more accurate than previous methods, as stated in the Declaration.

Based on the foregoing amendments and arguments, Applicants request withdrawal of this rejection under 35 U.S.C. § 103(a).

Claims 14, 15, and 17 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Chan *et al.* in view of Hirabayashi *et al.* and further in view of Brennan *et al.* (U.S. 2003/0232382). Applicants request reconsideration in light of the amendments and arguments presented herein.

The Office asserts that Brennan *et al.* disclose means for separating reactants of one reaction from another, including mechanical, chemical, or combination methods (Office action, page 6, last paragraph). The Office acknowledges that Brennan *et al.* do not teach applying a rubber having one or more holes to a glass substrate to define the reaction well. However, the

Office asserts that modifying the biosensor of Chan *et al.* by Brennan *et al.* results in a device where a layer of rubber is attached to a glass substrate to define reaction wells, would have been obvious to one of skill in the art because Brennan *et al.* disclose that use of materials such as rubber were well known in the art (Office action, page 7, first full paragraph).

Claim 14 is amended herein to recite a "glass substrate …in which a number of reaction vessels have been formed by affixing a rubber having a number of holes onto the glass." Support for this amendment is found in the specification at least at page 5, lines 33-36. New claim 34 is added, which recites "wherein the rubber is a black silicon rubber." Support for this claim is found in the specification at least at page 22, lines 30-34.

As acknowledged by the Office, Brennan *et al.* does not disclose affixing a rubber having a number of holes to a glass substrate to form reaction vessels. Further, as discussed above, Chan *et al.* disclose a porous semiconductor substrate and one or more coupled probes (*e.g.,* Chan, Abstract and paragraph [0013]). Chan *et al.* do not disclose a glass substrate, let alone a "glass substrate coated with a compound comprising an epoxy group as an active group, onto which a protein that interacts with a sugar chain has been immobilized…" as in Applicants' claim 14. Thus, the combination of Brennan *et al.* and Chan *et al.* does not result in the glass substrate of claim 14 and would not have been obvious to one of skill in the art in light of these references.

Furthermore, as set forth in the Declaration of Dr. Hirabayashi (paragraphs 15-16), use of a glass substrate and a rubber sheet with multiple holes affixed to the glass substrate is highly advantageous. This combination permits formation of a microarray with multiple wells, allowing a high-throughput system, and the rubber does not interfere with formation of the evanescent wave generated by injection of the excitation light from the edge of the glass substrate.

Based on the foregoing arguments and amendments, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 103(a).

Conclusion

Applicants respectfully submit that the claims are now in condition for allowance and such action is requested. If any issues remain, the Examiner is requested to contact the undersigned to arrange a telephonic interview prior to the preparation of any further written action.

Respectfully submitted,

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